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Respiratory system

Exchange of gasses occurs at 2 levels :

- 1 Internal respiration (cellular resp) use of O_2 at mitochondria to form.
- 2 External respiration exchange of O_2 & CO_2 between atmosphere & body tissues. It involves respiratory & circulatory system. It involves 4 processes:
 - a Pulmonary ventilation i.e. inspiration and expiration.
 - b Exchange of O_2 & CO_2 at alveoli by diffusion.
 - c Transport of O_2 & CO_2 to tissue by blood.
 - d Exchange of O_2 & CO_2 at tissues by diffusion.

Non respiratory Functions of lungs : ^{oral / written} ~~important~~ important.

- 1 Regulation of acid-base balance in blood.
- 2 Route of H_2O & heat losses viz expired air.
- 3 Defense against pathogens & foreign particles in airways.
- 4 Helps venous ^{conformity to heart} return (via resp. pump).
- 5 Activation of certain plasma proteins e.g. Angiotensinogen.
- 6 Enabling vocalization.

Organization of respiratory system ^{قراوة} MCA

Trachea branches into 2 bronchi each gives more than 20 generations of

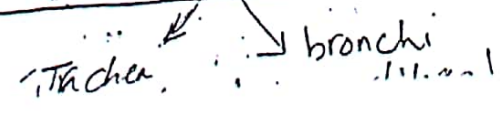
- Wall of trachea and bronchi contain cartilage
- Wall of bronchioles has no cartilage MCA.
- Alveoli begin in respiratory bronchioles, more in alveolar duct $\rightarrow$ Alveoli

Air way smooth muscles are supplied by :

- a Vagal cholinergic fibres which causes bronchoconstriction
- b Sympathetic adrenergic fibres (β_2) which causes bronchodilation

Air way beyond the larynx can be divided into two zones

- ① Conducting zone
NO Alveoli i.e. no exchange
- ② Respiratory zones
From resp. bronchioles down to Alveoli and Alveolar ducts (no exchange)



Respiratory

VISIT...

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a Warms & humidifies insp. air (Canada) Function • Gas exchange

b Distributes air to resp. zone (الكويبة)

IN/ Defend alveoli from microorganism, dusts, particles & noxious gases. (مخبر)
Air way to end of resp. bronchioles contains cilia i.e. mucus escalator (مخبر)

Alveolar macrophages engulf inhaled particles and bacteria
Cigarette smoke immobilizes cilia for hours & injures macrophage

Most alveoli are clustered into alveolar sacs & have 3 types of cells

- 1 Type I alveolar cells (pneumocytes) Single layer of squamous epith.
- 2 Type II alveolar cells (type II pneumocytes) secrete surfactant
- 3 Alveolar macrophages. Dead macrophages are moved from the alveoli to conducting zone & carried by mucus escalator to pharynx where they can be swallowed with mucus.

Air way epith. secretes a watery fluid upon which mucus ride freely

Particles $> 10 \mu m$ are trapped on hairs & moist mucus in nasal passages.

Particles $< 10 \mu m$ are inhaled in lung & stick on mucous film at every bend in airway & pushed towards pharynx by cilia (upwards to entrance).

2nd protective mechanism below bronchioles & in alveoli is macrophages

In many places in lungs, basement membranes alveolar epithelial cells and capill. endothelial cells fuse to form resp. membrane (0.2 μ) thick

Total area of 300 million alveoli in both lungs = $100 m^2$ (tennis court)

Each lung is surrounded by 2 layers of completely closed sac (pleural sac)

Between 2 layers of pleura is the intrapleural space filled with a very thin fluid film (15 ml) mostly water. This volume remains constant when chest wall expands and contracts; as water is incompressible

Pulmonary ventilation and pulmonary pressures: $P_1 - P_2$

$$F \text{ (Flow)} = \frac{P(\text{atmospheric}) - P(\text{alveolar})}{R \text{ resistance of airways}}$$

For simplicity, all respiratory pressures are expressed relative to atmosph. p. which is considered 0 and not 760 mmHg. (2)

Pulmonary pressures

1 Intra-Alveolar Pressure = intrapulmonary p

Mid inspiration $P(\text{alv.}) = -1 \text{ mmHg}$

Mid expiration $P(\text{alv.}) = +1 \text{ mmHg}$

End of insp. or exp. $P(\text{alv.}) = 0 \text{ mmHg}$

2 Intra-Pleural Pressure = intrathoracic p (بشكل 5 نقط)

① Def -ve p. between 2 layers of pleura

-ve p. inside pleural sac

② Cause Continuous tendency of lungs to recoil & chest wall to expand.

Causes of recoil tendency of lungs

Expansion tendency of chest

1 Elasticity of lungs ($\frac{1}{3}$ force)

Elasticity of chest wall

2 Surface tension of fluid

lining alveoli ($\frac{2}{3}$ force)

At end of normal expiration, when all resp. ms are relaxed.

both lungs and chest wall volumes are 2.5 litre.

While relaxation vol. of lungs 1L & relax vol. of chest wall 5L

③ Measurement Intraesophageal balloon connected to sensitive manometer

At end of normal expiration -- 4 mmHg.

At end of normal inspiration -- 6 to -8 mmHg.

Muller's experiment: forced insp. against closed glottis -30 to -40 mmHg

Valsalva " i.e. forced exp. against closed glottis +ve i.e. +50 mmHg

← Newly born (relax vol of lung = relax vol of chest) so pleural p = 0

④ Functions : It helps lung expansion (it prevents lung collapse)

: It helps venous & lymphatic return to heart

⑤ Intrapleural p. becomes +ve during Valsalva experiment

and in Pneumothorax : Presence of air in pleural space.

Types : External (open) pneumothorax : knife or gunshot

2 Internal (closed) pneumothorax : damage of pleura by lung disease

Curve. على نصف الدرجة

Effects of pneumothorax 1 lung recoils & chest wall expands

2 Decreased venous return and lymph flow

[3] Transpulmonary Pressure = $P(\text{alv.}) - P(\text{i.p.})$ MCQ

It is the difference in pressure between intralveolar & intrapleural P.

It is the distending (expanding) force of lungs i.e it opposes lung elastic recoil.

At end of expir. = $0 - (-4) = 4$ At end of insp. = $0 - (-8) = 8 \text{ mmHg}$

Pulmonary surfactant is a surface active agent.

• Chemical nature phospholipid (dipalmitoyl lecithin) + apoproteins + Ca^{++} ions

• Function Lecithin $--$ surface tension of fluid lining alveoli

Apoproteins & Ca^{++} ions $++$ spread of lecithin to $++$ its effectiveness.

Thus, surfactant Facilitates lung expansion

2 Prevents ^{small} alveolar collapse during expiration (as its conc. is $++$)

3 Prevents pulmonary edema. (by $--$ filtering force from bl. into alveoli)

• It is secreted by type II alveolar cells (type II pneumocytes)

• Surfactant deficiency occurs in :

1 Respiratory distress syndrome RDS = Hyaline membrane disease.

It occurs only in premature babies (2nd cause of death in prematures)

2 Long term inhalation of 100% O_2 or pump oxygenation in cardiac surgery

3 Cigarette smoking

4 Occlusion of one pulmonary artery.

5 Hypo thyroidism

6 Hypo corticoidism

7 Hyper insulinism

Mechanism of respiration.

inspiration, expiration and resp. pause

Inspiration	Expiration
Active process $++$ in all (3) dimensions Distension (inflate) Negative -759 mmHg Rushes in	Normally, passive (without muscle contraction) $--$ in all its dimensions Recoil (deflate) Positive $+1 \text{ mmHg}$ Forced out

المواد ينتقل من الضغط العالي إلى المنخفض

Expiration.

dir

inspiratory muscles

descend

Diaphragm

cont ++ vertical dimension (75%) ++ in thoracic vol)

External intercostals

cont → Elevation & Eversion of ribs

transverse & antero-posterior diameters

inspiration

++

Accessory insp. ms i.e. Sternomastoid, Scaleni, Serratus anterior

contract only with forced inspiration

Expiratory muscles

Abdom. ms & Internal intercostals contract only with forced expiration.

Compliance (C)

Any hollow elastic structure tends to expand as pressure difference across its wall i.e. distending pressure = transmural p becomes +ve is increases. If transmural p becomes -ve i.e. -- the hollow organ collapses.

$$\text{Compliance (C)} = \Delta V / \Delta P \quad (P_{\text{inside}} - P_{\text{outside}})$$

Definition change in vol per unit change in distending pressure

Compliance of lungs Static lung compliance
Total C of both lungs in a normal adult = 200 ml air/cm H₂O

Lung compliance Hysteresis loop
Lung vol changes is plotted against transpulmonary p in excised lung of a cat.

Transpulmonary p is changes in small steps during both inflation and deflation. and lung vol is allowed to come to a steady level each s.

Hysteresis shape is due to change in surfactant molecules concentration in alveoli i.e. ++ by deflation → -- surface tension & vice versa

So, compliance ++ by deflation & -- by inflation.

Compliance force of lungs opposes recoil forces of lungs:

- Elastic force $\frac{1}{3}$. Surface tension of fluid lining alveoli.
Prove P need to expand air filled lung is 3 times p. requ to expand saline filled lung (where surface tension effect is eliminated)

quiet breathing

• Factors affecting compliance of lungs:

- | | |
|---|---|
| 1 <u>Decreased in</u> | 2 <u>Increased in</u> |
| a) <u>Restrictive lung diseases</u>
e.g pulm congestion & fibrosis | a) <u>Old age</u> |
| b) <u>Deficiency of surfactant</u> e.g RDS | b) <u>Emphysema</u> : Alv. wall break
→ alveoli replaced by large spaces |

• Functional significance of abnormally high or abnormally low C:

- 1 low C indicates stiff lung and increased work of breathing.
- 2 high C e.g emphysema no problem in inflating lungs but have extreme difficulting exhaling air i.e extra work is required

[B] Compliance of thoracic wall and lung together dynamic lung compliance

- It equals 110 ml air / cm H₂O p.
- It is measured in living subject
- Frictional resistance to air is relatively small during quiet breathing but it causes pleural p changes to precede lung volume changes

• Factors affecting compliance of thoracic wall:

- | | |
|---|------------------------|
| 1 <u>Decreased in:</u> | 2 <u>Increased in:</u> |
| a sk ms diseases e.g myositis & poliomyelitis | a athletes |
| b arthritis and kyphoscoliosis | |
| c obesity | |

Work of breathing

During quiet breathing, resp. ms perform work only during inspiration
Work of breathing is divided into three fractions

<u>Work. (W)</u>	<u>Work required to overcome</u>	<u>Represents</u>
1 <u>Compliance or elastic W</u>	recoil forces [elasticity, surface tension]	Most of work
2 <u>Tissue resistance work</u>	viscosity of lungs & chest wall	least of work
3 <u>Airway resistance work</u>	airway resistance	

Notes • During heavy breathing or when airway or tissue resistance is great, expiration work does occur e.g br. asthma. (6)

Quiet breathing consumes 5% of total energy expenditure by body
During heavy exercise breathing consumes 20% of total energy

Airway resistance $\propto \frac{1}{\text{cross sectional area of air passages}}$

Greatest resistance in medium-sized bronchi

Small bronchioles are enormous in number & have large cross sectional area

Factors affecting diameter of airway passages:

A) Factors causing bronchodilation B) Factors causing bronchoconstr.

1. Sympathetic stim. β_2 receptors

1 Vagal stim. Muscarinic R

2 ++ lung volume

2 -- Alveolar PCO_2 direct eff

→ traction on walls of airway

3 Histamine in allergy

•
$$F(\text{Flow}) = \frac{\Delta P (\text{Pressure difference})}{R (\text{Resistance})}$$

• Work of breathing is increased by decreased $\leftarrow$ Surfactant
diameter of airways

Pulmonary ventilation

Over time, the volume inspired equals the volume expired.

There are 4 pulm. volumes and 4 pulm. capacities

Following vol. obtained from σ adult 70 Kg sitting at rest In σ 10% less

Pulmonary volumes: 4 non-overlapping lung volumes

1 Tidal volume (V_T) vol insp. or exp. each cycle during rest = 500 ml

2 Inspiratory reserve volume (IRV) Maximal vol. insp. after normal insp = 3000 ml

3 Expiratory reserve volume (ERV) Maximal vol. exp. after normal exp. = 1200 ml

The above volumes are measured by a spirometer (air chamber inverted over water chamber) It contains air or O_2 . Technique = Spirometry Record = Spirogram

4 Residual volume (RV) vol. remaining in lungs after maximal expir. = 1200 ml

It is not measured by the spirometer It is measured by helium dilution method

Lung capacities: sums of 2 or more of lung volumes 4 capacities

1 Inspiratory capacity (IC) Maximal vol. insp. at the end of resting expiration

$$IC = V_T + IRV = 3500 \text{ ml.}$$

(7)

Functional residual capacity (FRC) vol. remaining in lungs after normal expiration

$$FRC = ERV + RV = 2300 \text{ ml}$$

Vital capacity (VC) Maximal vol. exp. after maximal insp.

$$VC = V_T + IRV + ERV = 4600 \text{ ml}$$

4 Total lung capacity (TLC) vol. of air in lung at the end of maximal insp.

$$TLC = V_T + IRV + ERV + RV = 5800 \text{ ml}$$

Determination of RV, FRC and TLC: not measured by spirometer

Helium dilution method measures FRC

Helium is an inert insoluble gas not used by body, so

amount of helium before exper. = amount of helium after experiment

amount of helium in spirometer = „ of helium in spirometer + lungs

$$C_1 \times V_1 (\text{vol of spirometer}) = C_2 \times V_2 (\text{vol of spirometer} + \text{FRC})$$

C_1 conc. of helium in „ before C_2 conc. of helium in „ after exp

Test begins at end of normal expir. (FRC), & lungs contain no helium
(all helium in spirometer which is filled with 40% helium in air)

Subject breathes 3 to 4 times the helium - air mixture.

Since FRC is the only unknown in the equation, FRC is easily determined.

$$RV = FRC - ERV \quad \text{and} \quad TLC = FRC + IC$$

N.B Minimal air: Few cc's of air that remains in lungs after opening of chest wall & loss of -ve pleural p and collapse of lung.

Medicolegal importance Minimal air is present only on infant born alive
not in infant born dead (still birth) where it allows floating of
of lung tissues if placed in water

Factors affecting vital capacity

1 Physiological:

++ VC Males Athletes, Standing position

-- VC Females Old age, Recumbent position, Pregnancy

2 Pathological: (Clinical significance)

VC is an index of physical fitness, so VC decreases in Chest wall diseases

a Resp. ms : myositis or paralysis

b Bones : Kyphosis or scoliosis

Lung diseases

a Restrictive : lung fibrosis

b Obstructive : Asthma or emphysema.

Abdominal

Ascitis or tumour

Time vital capacity

The subject inspires maximally & then exhales as hard & as complete as he can.

The vol exhaled in 1st second is forced expiratory volume in one second FEV_1

Total volume exhaled is forced vital capacity or FVC (slightly less than VC)

Normally, FEV_1 is 80% of FVC.

In restrictive lung diseases	In obstructive lung diseases
e.g Pulmonary fibrosis	e.g bronchial asthma
Both FEV_1 & FVC --	FEV_1 -- more than FVC --
FEV_1 / FVC % normal or ++	so FEV_1 / FVC % is low

Alveolar ventilation

Minute ventilation (minute resp. volume) = $TV \times \text{Resp. rate / minute}$

$$= 500 \times 12 = 6000 \text{ ml / min} = 6 \text{ Litre / min.}$$

Dead space DS

Definition Vol of air in resp. system that doesn't undergo gas exchange.

Types of DS

1 Anatomic DS = Conducting zone = $\frac{1}{3}$ i.e 30% of tidal volume

2 Alveolar DS i.e nonfunctioning alveoli (have no bl. supply)

3 Physiologic DS = Anatomic DS + Alveolar DS

In normal person, physiologic DS = anatomical DS

Measurement of dead space

1 Measurement of anatomic DS : Fowler's method (single breath N_2 test)

Subject takes a deep breath of pure O_2 then expires in a rapidly (9)

- recording N_2 meter. N_2 conc. rises as DS gas is increasingly washed out by alveolar gas. Finally, uniform N_2 conc represents pure alv. gas. DS volume is found out by plotting N_2 conc. against expired air volume & drawing a vertical line so that area A = area B (look curve). DS volume is the volume expired up to the vertical line.
- 2 Measurement of the physiologic (total) DS volume. Bohr equation

$$DS = \frac{P_a CO_2 - P_E CO_2}{P_a CO_2} \times TV \text{ (tidal volume)}$$

$P_a CO_2$ = partial p of CO_2 in arterial blood

$P_E CO_2$ = average partial p of CO_2 in entire expired air

Normal DS 150 - 166 ml i.e $\frac{1}{3}$ tidal volume.

Significance of DS

- 1 Alveolar (functional) ventilation does not equal pulmonary ventilation (minute respiratory volume)

Alveolar ventilation = (Tidal vol - DS) Respiratory rate

It explains difference in composition between alveolar air and expired air (mixture of alveol. air & DS) so it has more PO_2 & less PCO_2

- 2 Diseases & drugs causing rapid shallow breathing result in:

- Minute resp. volume: may be normal
- Alveolar ventilation: markedly reduced $\rightarrow$ Hypoxic Hypoxia

Importance of anatomical DS Discuss function of conducting zones

Exchange of gases in lungs

+ Page 38 $\rightarrow$ 38, 39, 40

Atmospheric air consists of N_2 79%, O_2 20.96% & CO_2 0.04%

Alveolar air consists of N_2 79.6%, O_2 14.8% & CO_2 5.6%

$$\begin{aligned} \text{Total dry p} &= \text{Atmospheric p} - H_2O \text{ vapour p at } 37^\circ C (47 \text{ mmHg}) \\ &= 760 - 47 = 713 \text{ mmHg} \end{aligned}$$

$$\text{Partial p of a gas} = \text{Total dry p} \times \% \text{ of gas in the gas mixture (10)}$$

$$P_{CO_2} \text{ in alveolar air} = \frac{713 \times 5.6}{100} = 40 \text{ mmHg}$$

Diffusion of gases:

A In gaseous media: Outside body.
 $DR \propto \frac{(P_1 - P_2)}{\sqrt{M}} \times \frac{T}{L} \times A$ refer to introduction.

So, DR of $O_2 : CO_2 = 1.2 : 1$
explanation M of $O_2 = 32$, M of $CO_2 = 44$.

B In aqueous media (physical solution) Inside body.

Partial p of a gas in solution is determined by:

- 1 Number of molecules of gas dissolved.
- 2 Solubility of gas in liquids vol of gas dissolved in 1 ml. It depends on nature of gas, nature of liquid, temp of liquid & p of gas.

Solubility coefficient

It is volume of a gas dissolved in 1 ml liquid when partial p. of gas is one atmosphere.

For $CO_2 = 0.57 \text{ ml}$, $O_2 = 0.024 \text{ ml}$ & $N_2 = 0.012 \text{ ml}$

i.e CO_2 is 24 times more soluble in water than O_2

Thus, CO_2 diffuses 20 times in water that does O_2 .

Respiratory membrane: 0.2μ is formed of 6 layers

- | | |
|-------------------------------|-------------------------------------|
| 1 Fluid containing surfactant | 4 Fluid of thin interstitial space. |
| 2 Alveolar epithelium | 5 Capillary endothelium. |
| 3 Epith. basement membrane | 6 Endothelial basement membrane. |

Blood traverses one pulm. capill in 0.75 second.

In resting conditions, complete equilibration occurs in 0.25 second.

For both O_2 and CO_2 in spite of higher solubility of CO_2 due to:

- 1 Pressure gradient of $O_2 : CO_2 = 60 : 5 \text{ mmHg}$.
- 2 CO_2 is transported in blood primarily as bicarbonate & carbamino compounds. It takes time to be reversed to free CO_2 (11)

$$\begin{array}{ccc} \uparrow & 40 & 105 \\ & 46 & 40 \end{array} \quad \begin{array}{c} 20 \\ 14.8 \end{array} \quad \begin{array}{c} 0.04 \\ 5.6 \end{array}$$

Factors that affect gas diffusion through respiratory membrane:

• The rate of diffusion is directly proportional to:

[1] Pressure gradient across alveolar-capillary membrane

	Arterial (Alveolar) P		Venous (tissue) P	P. gradient
O ₂	100	→	40	60 mmHg
CO ₂	40	←	46	6 mmHg

[2] Surface area

100 square meter

-- e.g in emphysema and collapse of lungs

++ in exercise due to opening of new capill & dilatation of opened capill

[3] Temperature

[4] Solubility of gas in medium

CO₂ : O₂

24 : 1

• The rate of diffusion is inversely proportional to:

[1] The square root of molecular weight CO₂ : O₂

1.2 : 1

[2] Thickness of membrane

0.2 μ

6 layers (discuss)

++ with edema & fibrosis of lungs.

• Alveolar Ventilation (V_A) Perfusion (Q) (V_A/Q) Ratio

- Def Ratio of Alveolar ventilation 4 L/min and pulm perfusion (COP of Rt ventricle) 5 L/min $\frac{4}{5} = 0.8$ average

- It is not uniform for all lung parts.

• Lung apex relatively poor bl. flow → high V_A/Q 3

• Lung base " high bl flow → Low V_A/Q 0.6

- Causes of regional differences in lung ventilation

Due to laws of physics, at lung base the intrapleural p is less -ve than at apex → more change in volume at lung base → more ventilat

At apex pleural p is more -ve → change in volume → less "

- Causes of regional differences in lung perfusion

At lung apex, pulm. capill p in standing position (due to gravitational effect) falls below alveolar p → capillaries nearly close → -- bl flow

$$O_2 \rightarrow 14.8 \times 713$$

$$105 \quad 40$$

$$CO_2 \rightarrow 5.6 \times 713$$

$$40 \quad 46$$

At lung base, pulm. capill. p. increases $\rightarrow$ ++ bl. flow.

Assessment of regional ventilation and perfusion:

Using radioactive xenon & monitoring for radioactivity over chest

. To test evenness of ventilation, a breath of xenon is inhaled.

. To " " of alveolar perfusion, xenon is injected intravenously

- Variation in V_A/Q

. V_A/Q ++ by -- bl flow e.g. occlusion of a vessel by a thrombus

. V_A/Q -- by -- ventil. e.g. " of a bronchi with emphysema

Effect of 2 extremes of V_A/Q submatching on alveolar & bl. gases:

[1] Normal perfusion, but no alveolar ventilation $V_A = 0$ e.g. br. obstruction

$V_A/Q = 0/Q = 0$ Atmospheric air does not reach the alveolus,

So alveolar PO_2 is 40 mmHg & PCO_2 is 46 mmHg i.e. similar to

venous bl. The venous capill blood will not be oxygenated.

This is called shunted blood.

[2] Normal ventilation, but no perfusion of Capill. $Q = 0$ e.g. pulm. thromb

$V_A/Q = V_A/0 = \infty$. The alveolar PO_2 152 mmHg & PCO_2 (0 mmHg)

is similar to inspired air, since no O_2 extracted or CO_2 added.

The ventilation in such alveoli is wasted.

- The cause of difference in PO_2 in arterial blood (100 mmHg) and alveolar air (105 mmHg):

1) 57% of blood comes from alveoli at lung base with low V_A/Q and

only 10% of blood " " " at lung apex with high V_A/Q

Therefore, the latter 10% can't compensate for the former 57%.

2) Physiologic shunt: Anatomic venous to arterial shunts i.e. 2-5%

of VR is not oxygenated and passes directly into systemic arterial bl.

- Venous bl. from upper airways collected by bronchial veins

- Coronary venous bl. passes from coronary veins to Lt vent directly

Autoregulation of V_A/Q by resp. gases Compensatory mech. matching V_A/Q

Ratio
(?)

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- 1 Alveolar Hypoxia -- PO_2 in capill draining poorly ventilated alveoli causes arteriolar VC $\rightarrow$ bl. shifts to the well ventilated alveoli.
- 2 Alveolar Hypocapnia -- PCO_2 in alveolar air due to over ventilation of alveoli or -- perfusion of alveoli causes airway constriction of these alveoli $\rightarrow$ air shift to the alveoli with a better V_A/Q

Oxygen transport by the blood

2 Forms:

- 1 O_2 in physical solution: $0.3 \text{ ml} / 100 \text{ ml}$ arterial blood
 $0.13 \text{ ml} / 100 \text{ ml}$ of venous bl. It is far below O_2 need by the body.
 It determines PO_2 in blood & in turn direction of diffusion of O_2
- 2 O_2 in chemical form with Hb $19.5 \text{ ml} / 100 \text{ ml}$ arterial blood.
 It constitutes the main supply of tissue (65 times the physical O_2).
 Each of the 4 ferrous atoms in Hb molecule combines reversibly with one O_2 mol.

Definitions:

- 1 O_2 content vol. of O_2 combined with Hb / 100 ml blood
 It depends on ① Hb content ② O_2 tension ③ Hb affinity to O_2
 ④ Metabolic state of organ.

- 2 O_2 capacity vol. of O_2 combined with Hb / 100 ml blood when Hb is fully saturated i.e. maximal vol. One gm of Hb combines with 1.34 ml of O_2 when it is fully saturated i.e. 15 g carries $20 \text{ ml } O_2$.
 It depends on Hb content.

- 3 % saturation of Hb with O_2 = $\frac{O_2 \text{ content}}{O_2 \text{ capacity}} \times 100$
 It depends on O_2 tension (not Hb content)

- 4 Coefficient of O_2 utilization by tissue
 = $\frac{O_2 \text{ content in arterial bl} - O_2 \text{ content in venous bl}}{O_2 \text{ content in arterial bl}} \times 100$

The hemoglobin O_2 dissociation curves

$\% Hb O_2$ is plotted against PO_2
 Hb O_2 dissociation curves are not linear but S (sigmoid) shape.

Hb O₂

0.3 19.5

1.34 20

15 20

50 Hb

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Hb O₂ saturation (not O₂ content) is used in curve because
 Hb O₂ " does not change with variation in Hb content (eg anemia)

t PO ₂	<u>20</u>	<u>40</u>	<u>60</u>	<u>100</u> mmHg
% Hb O ₂ sat.	<u>30%</u>	<u>70%</u>	<u>90%</u>	<u>97%</u>
	At <u>Lower</u> tension < 60 mmHg i.e at Tissues Curve has its <u>steep</u> part Affinity of Hb to O ₂ is <u>low</u> i.e unloading of remaining 3 O ₂ molecules is progressively easier		At <u>Higher</u> tension > 60 mmHg i.e at Lungs Curve is <u>Horizontal</u> (Flat part) Affinity of Hb to O ₂ is <u>High</u> i.e unloading of 1st O ₂ molecule requires marked decline in PO ₂	

N.B Curve is S shape; because it has Flat & steep parts (discuss)

Coefficient of O₂ utilization during rest 25% reaches 75% in exercise

Coefficient of O₂ " $\propto$ $\frac{\text{Metabolic activity of tissues}}{\text{Rate of blood flow to tissues}}$

P₅₀: PO₂ at which Hb is 50% saturated. Normally 27 mmHg

P₅₀ is inverse function of Hb affinity to O₂

i.e at higher affinity (curve shift to left) P₅₀ decreases

Factors affecting oxyhemoglobin dissociation curve

	Shift to right Decreased affinity Increased P ₅₀ Increased t. activity	Shift to left Increased affinity Decreased P ₅₀ Decreased t. activity
1 PCO ₂	++	--
2 [H ⁺]	++	--
3 Temperature	++	--
4 2,3 DPG	++	--
		CO poisoning (15)

Causes for shift to right

2,3 DPG is end product of glycolysis in RBCs.

It increases in case of hypoxia (High altitudes) or exercise.

DPG, CO_2 and H^+ combine with sites on Hb changing its configuration and facilitating off loading of O_2 (unloading).

Once Hb is partially unsaturated Hb binds H^+ , CO_2 & DPG

→ unloading of O_2 & provides more O_2 to tissue with ++ metabolism

Effect of CO (carbon monoxide) on O_2 dissociation curve.

Affinity of CO for O_2 binding sites on Hb 200 times that of O_2

O_2 binding sites occupied by CO don't respond to -- PO_2 & O_2 remain strongly bound to Hb i.e. curve is shifted to left

Adult Hb (Hb A) & Fetal Hb (Hb F): refer to blood page 3

Hb A beta polypeptide chains can combine with 2,3 DPG → --

affinity of Hb to O_2 . Hb F gamma polypeptide chains can't combine with 2,3 DPG → ++ affinity of Hb to O_2 i.e. shift to left

O_2 dissociation curve of myoglobin:

Myoglobin (unlike Hb which has 4 Fe^{++} atoms) has one ferrous atom which can combine with one O_2 molecules.

O_2 dissociation curve for myoglobin is rectangular/hyperbolic.

i.e. it remains horizontal till very low O_2 tension i.e. it does not give its O_2 except at very low O_2 tension e.g. during severe exercise when curve suddenly descends vertically. So, myoglobin acts

as small store for O_2 . After exercise, myoglobin takes O_2

from blood Hb. Neither Hb, nor myoglobin can carry function of each other.

• Bohr effect: Effect of PCO_2 and pH on oxy Hb diss. curve

i.e. ++ PCO_2 & -- pH decrease O_2 binding to Hb → shift to right

CO₂ transport by blood

arterial blood → 19.67 ml %
venous blood → 14 ml %
tissue take up → 5.4 ml %
O₂ given to tissue = 19.67 - 14 = 5.67
dissolved in plasma H₂O

Total CO₂
Arterial CO₂
in 100 ml bl

Tidal CO₂

CO₂ given by tissues
to 100 ml bl.

48 ml

4 ml

1 Physically dissolved

2 Chemical combination

a Bicarbonate

b Carb amino compound

- Hb - NHCOOH

- Pln - NHCOOH

3 5%

42 89%

3 6%

4% (Hb)

2% (plasma pln)

0.4 10%

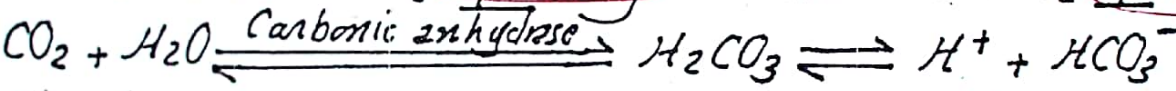
2.6 65%

1 25%

Venous bl CO₂ = Total CO₂ + Tidal CO₂ same/100ml

CO₂ in physical solution is responsible for PCO₂ in blood.

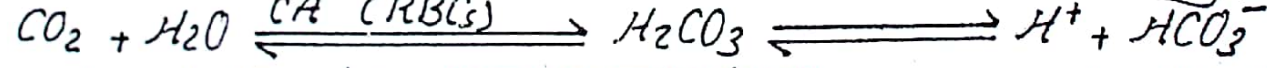
In arterial bl. PCO₂ 40 mmHg In venous bl. PCO₂ 46 mmHg



The above reaction is very slow in plasma (no CA), but several thousand times faster in RBCs because of presence of CA enzyme

CO₂ carriage at TISSUES Cl shift (Hamburger) phenomenon.

CO₂ diffuses from tissues (PCO₂ 46) to blood PCO₂ 40 mmHg.



H⁺ is buffered by deoxy (reduced) Hb in RBCs (Hb - NHCOOH)

and by plasma plns in Plasma (Pln - NHCOOH)

HCO₃⁻ diffuses from RBC to plasma along its electrochemical gradient.

So HCO₃⁻ is buffered by Na⁺ in plasma (75%)

as well as by K⁺ in RBCs (25%)

N.B RBCs membrane is impermeable to cations (K⁺ & Na⁺)

Cl⁻ diffuses from plasma to RBCs to maintain electrical balance (17)

(neutrality) i.e. Cl⁻ - bicarbonate exchange continues until.

$$\frac{HCO_3^- \text{ Plasma}}{HCO_3^- \text{ RBCs}} = \frac{Cl^- \text{ RBCs}}{Cl^- \text{ Plasma}} \quad \text{Donnan's equilibrium}$$

N.B At the LUNGS opposite effects occur

Results of Cl^- shift	At TISSUES		At LUNGS	
	<u>RBCs</u>	<u>Plasma</u>	<u>RBCs</u>	<u>Plasma</u>
1 <u>HCO_3^-</u>	+	+	-	-
2 <u>Cl^-</u>	+	-	-	+
3 <u>Kations</u>	$\pm$	$\pm$	$\pm$	$\pm$
4 <u>OP</u>	++	$\pm$	--	$\pm$
5 <u>H_2O shift</u>	$\leftarrow$		$\rightarrow$	
6 <u>PCV (HV)</u>	+		-	
7 <u>pH of blood</u>	slightly <u>decreased</u>		slightly <u>increased</u>	

(N.B) Most of tidal CO_2 is carried as HCO_3^- 2.6 ml mostly $NaHCO_3$, 1 ml as carbamino compounds (discuss) & 0.4 ml dissolved.

CO_2 dissociation curves (oxygenated & deoxygenated blood)

CO_2 content in blood is plotted against blood PCO_2

In physiologic PCO_2 range 40-46 mmHg, CO_2 curves are linear

- Arterial bl. has CO_2 content 48 ml % & PCO_2 40 mmHg.

- Venous bl has CO_2 content 52 ml % & PCO_2 46 mmHg.

Although CO_2 & O_2 are carried at different sites by Hb (CO_2 with Fe^{2+} and CO_2 with NH_2) yet binding of one of them with Hb -- binding of other

Bohr effect ++ CO_2 in bl causes displacement of O_2 from Hb

Haldene ,, binding of O_2 with Hb causes ,, of CO_2 from Hb

Pulmonary function tests

For working ability & physical fitness

[1] Pulmonary vent. tests i.e resp. minute vol & alveolar ventilation
discussed before page Important in shallow rapid breathing.

[2] Static lung volumes some of lung volumes & capacities (18)

include $RV + VC = TLC$ and ERV
Also, Physiologic (total) DS , compliance of lung & chest & V_A/Q
Dynamic lung volumes measure volumes / unit time

[1] Maximal breathing capacity (MBC) = Max. Vent. volume (MVV)

Def Max vol insp or exp / min. by deepest & fastest breathing
Measurement Using respirometer for 15 sec. then multiply by 4
to avoid muscle fatigue and development of resp. alkalosis

Normal range Adult men 80-170 L/min Adult ♀ 60-120 L/min

Factors affecting Same as factors affecting VC

Again, MBC like VC declines by age.

Significance Better index than VC for physical fitness

VC may be normal while MBC (repeated VC) is decreased.

MBC shows power of resp centre & ms to do maintained effort.

[2] Breathing reserve (BR) = $MBC - \text{resp minute vol.}$

Dyspnoic index $DI = \frac{BR}{MBC} \times 100$

Normally DI is more than 90%.

In dyspnea, DI is less than 70%.

[3] Timed vital capacity (Forced expiratory volume) FEV

FEV_1 % vol of expired air at end of 1st-second to VC.

Discussed before page

[4] Maximum Flow rate. i.e. Maximum velocity of expired air

Measurement Peak Flow meter.

Significance decreased in obstructive lung diseases

[5] Assessment of regional ventilation & perfusion

Discussed before See (V_A/Q) page

Good Luck

Control of respiration

Respiratory muscles are typical sk ms requiring stim. from CNS.
There are 2 separate neural control system for respiration

A Voluntary control: Generated from neurones in cerebral cortex.
Reaches resp. motor neurones via corticospinal & corticobulbar tracts.
Importance for voluntary acts as talking, singing & breath holding

B Involuntary control: Generated from spontaneously discharging neurones in pons and medulla known as respiratory centres.
Located bilaterally (on both sides) in Pons & Medulla
Contain inspiratory & expiratory neurones with reciprocal innervation
Medullary respiratory centres

2

Dorsal respir. group (DRG)

Dorso-medial position in medulla

Composed of inspir. neurones only

Located in nucleus tractus solitarius

Sensory afferent terminations of
IX & X nerves for mechano, baro
and chemoreceptors

It has inherent rhythm i.e. pace-

maker (depol. spontaneous & rhythmic)

Receives excitat. impulses from A.P.C.

& inhib. impulses from lung stretch R.

Sends Insp. ms (i.e. Diaphragm

& ext. intercostal ms during eupnea

To VRG during forced breathing

Ventral respir. group (VRG)

Ventral-lateral position in medulla

Composed of inspir & expir neurones

Located in nucleus ambiguus

and retroambiguus

It has no rhythm

Inactive in quiet normal breathing

Receives excitat. impulses from DRG

at higher level of pulm. ventilation

Sends to accessory insp. ms during

forced inspir. & to expiratory ms

during forced expiration

Note Inspir. ramp signals: DRG sends gradual (ramp) insp. A. potent
for 2 sec. then stops abruptly for 3 sec to allow passive expir. (1)

Medullary centres alone produces rhythmic slow irregular respiration. Their activity is modified by pontine respiratory centres.
Pons

Pneumotaxic centre PNC

lies in upper pons.

OFF SWITCH It sends inhibitory impulses to A.P.C.

It is slower than vagal inhibition

Limits duration of inspiration

Apneustic centre APC

lies in lower pons

ON SWITCH It sends regular continuous signals to DRG

It sends excitat. impulses to PNC

Increases duration of inspiration

Note APC receives inhibitory impulses from lung stretch receptors along vagal afferents & PNC (slower than vagal inhibition).

APC stimulates → PNC -ve feedback (inhibition) → APC

APC & PNC regulate the rate and depth of respiration.

Role of the vagus nerve

2nd OFF SWITCH is Lung stretch receptors which transmit inhibitory impulses to APC & DRG along VAGUS (Hering Breuer reflex)

Together with PNC, it adjusts switch off point at tidal vol. 500 ml

It is particularly active in animals, infants at high rate and depth of respiration e.g. during exercise when tidal vol > 1000 ml

When APC is inhibited, insp. ms are turned off → passive expir.

Genesis of rhythmic respiration:

- APC sends excitatory impulses to DRG.
- DRG sends „ impulses to Diaphragm and External intercostal ms → inspiration
- OFF SWITCHES PNC & Hering Breuer Reflex send inhibitory impulses to stop inspir. at TV 500 ml (Discuss)
- Expiration follows passively.
- APC recovers from inhibition & cycle repeats itself. ②

2012/08/24

Experimental evidence

Cutting two vagi :: Respiration becomes slower and deeper.

Transection of brain stem at

- a Upper pons : No effect on involuntary (automatic) respiration
- b Mid pons : Slightly slower and deeper respiration.
- c Upper medulla : Rhythmic yet irregular and slower respiration.

Note Cutting both vagi doesn't affect inherent rhythmicity of resp.

d Lower medulla : Stoppage of breathing & death from resp. failure.

Note TS of sp. cord below C5 : Diaphragmatic respiration

3 Cutting two vagi plus TS at mid pons results in:

- Apneusis : breathing stops in full inspiration.
- Apneustic breathing : slow inspiratory spasms interrupted by intermittent expiration.

Regulation of respiration

- Aims :
- 1 Pulm ventilation is made proportional to metabolic needs
 - 2 Keep alveolar and arterial PCO_2 , $[H^+]$ & PO_2 constant
 - 3 Protect airway passages and lungs

Regulation involves 4 elements:

- 1 Sensors i.e. receptors
- 2 Central controller i.e. respiratory centres in brain stem
- 3 Effectors i.e. respiratory muscles
- 4 -ve feedback i.e. response has effect on original stimulus

Regulation of respiration

① Chemical regulation : basic mechanism for regulation of rhythmic resp.

② Non-chemical (nervous) regul. : Superimposed on basic chemical regul.

Chemical regulation of respiration basic mechanism.

• Resp. is stimulated by $++ PCO_2$, $++ [H^+]$ & $-- PO_2$ ③

- Opposite changes have slight inhibitory effects.
- In this way, pulm. ventilation $\propto$ body needs and PCO_2 , $[H^+]$ & PO_2 in arterial bl. are kept constant. The effects of changes in PCO_2 , H^+ & PO_2 are mediated via respiratory chemoreceptors (central & peripheral chemoreceptors)

• Central chemoreceptors Bilateral.

- Site beneath ventral surface of upper part of medulla. very close but separate from resp. centre neurones
- Stimulus increased PCO_2 (only) of arterial blood
- Mechanism Indirect via H^+ ions

Central chemoreceptors act as H^+ receptors
 $\therefore PCO_2$ in arterial bl. crosses blood brain barrier BBB
 $\rightarrow$ immediately $\therefore PCO_2$ (within 10 min) in CSF & brain interstitial F
Hydrated i.e. $CO_2 + H_2O \xrightarrow{\text{carbonic anhydrase}} H_2CO_3$
Dissociated $H_2CO_3 \longrightarrow HCO_3^- + H^+$

H^+ ions stimulate central chemoreceptors indirectly

Note CSF is not highly buffered (20 mg ptn / 100 ml) as plasma.

79 mg / 100 ml (7000 mg ptn / 100 ml) $\rightarrow$ larger change in CSF $[H^+]$ $\rightarrow$ strong stim.
 Severe hypoxia depresses CNS including resp centres & central chemoreceptors

• Peripheral chemoreceptors special chemoreceptors outside CNS

- Site: Aortic bodies in aortic arch
Carotid bodies bilaterally at bifurcation of common carotid art.
- Innervation: Buffer nerves
 - Aortic bodies : Vagus nerve
 - Carotid bodies : Glossopharyngeal nerve (Stierling's nerve)
- Stimuli:

1 Mainly by -- arterial PO_2 between 30-80 mmHg. (4)

Because peripheral chemoreceptors have high bl. flow 20 ml / min / gram

Blood

tissue; O_2 needs of their cells are met by dissolved O_2 alone.

So, they are sensitive to $-- O_2$ tension (PO_2) only and not to $-- O_2$ content in Hb and aren't stim in anemia, metHb CO poisoning. However, they are stim by $--$ bl flow as in hge $--$ ABP

2 $++$ arterial $[H^+]$ metabolic acidosis i.e. fixed acids

3 $++$ arterial PCO_2 (PCO_2 affects mainly central chemoreceptor)

* Peripheral chemoreceptors are particularly important in

1 Hypoxia ($PO_2 < 60$ mmHg).

2 Metabolic acidosis and alkalosis.

3 Depression of central chemoreceptors and respiratory centres by narcotics or anesthetic. Effect of CO_2 on central ch. is abolished.

Hypoxia on peripheral chemoreceptors become driving force for respir.

So, giving pure O_2 in such case will remove driving effect of $-- PO_2$ on respiration. To avoid this, Pt is put on artificial respirator

Resting chemical drive of resp. results from:

- 85% due to stimulatory effect of CO_2 on central chemoreceptors
- 15% due to stimulatory effect of O_2 on peripheral

Ventilatory response to O_2 Lack :

Hypoxia stimulates respiration via peripheral chemoreceptors

- At PO_2 100-70 mmHg : no increase in ventilation

Significance : Drop of PO_2 from 100 to 70 mmHg doesn't affect

% saturation of Hb with O_2 (plateau part of O_2 diss. curve)

- At PO_2 60 mmHg : ventilation is doubled
- At PO_2 30 mmHg : ventilation increases 6 times
- At PO_2 20 mmHg : direct inhibitory effect on resp. centre

Ventilatory response to CO_2 changes :

$++ PCO_2$ stimulates respiration via central chemoreceptors 80% and peripheral chemoreceptors 20% of ventilatory effect (5)

A small rise in PCO_2 e.g. $3\% CO_2$ will double vent $\rightarrow \pm PCO_2$
 $10\% CO_2$ will $++$ ventilation 10 times

Ventilatory response to $[H^+]$ i.e. to change in acid-base balance

$++ [H^+]$ of arterial blood will stimulate peripheral chemoreceptors

$$[H^+] \propto \frac{PCO_2}{HCO_3^-} \quad \text{i.e.} \quad \frac{\text{Physical } CO_2}{\text{Chemical } CO_2}$$

Acidosis = $++ [H^+]$ and Alkalosis = $-- [H^+]$
 H^+ ions of arterial blood can't cross blood brain barrier.

item \ type	Resp. acidosis	Metabolic acidosis	Resp. alkalosis	Metabolic alkalosis
Defect	$++ PCO_2$	$-- HCO_3^-$	$-- PCO_2$	$++ HCO_3^-$
Cause	Hypoventil. • depression of resp centre • lung diseases	Lactic acid in exercise Ketoacids in DM	Hyperventil. • anxiety • CNS disorders	severe vomiting treatment of peptic ulcer by HCO_3^-
Compensat.	Renal retain i.e. $++ HCO_3^-$	Respiratory Hypervent $-- PCO_2$	Renal excrete i.e. $-- HCO_3^-$	Respiratory Hypovent. $++ PCO_2$

O_2 lack is a weaker stimulus for respiration than CO_2 excess:

- Stimulating effect of hypoxia is opposed by inhibitory effects caused by $-- PCO_2$ & $-- [H^+]$ caused by hyperventilation.
 Again, in hypoxia deoxygenated Hb is a weaker acid than oxy Hb $\rightarrow$ less $++$ in $[H^+]$ $\rightarrow$ less stim. of peripheral chemorecept.
 These inhibitory effects balance effect of hypoxia between 70-100 mmHg
- Drop of PO_2 from 100 to 70 mmHg doesn't affect % saturation of Hb with O_2 while least changes in PCO_2 will affect pH & chemical reactions of cells

Nonchemical (NERVOUS) regulation:

- Afferents from higher centres Cerebral cortex (CC)
 CC can override function of resp. centres in brain stem within limits
 e.g. talking, singing, playing wind instruments & straining.
 Pathway 1 to resp. centre neurones in brain stem. (6)

or directly to spinal motor neurones of resp. muscles along corticospinal and bulbospinal trs.

Forms of voluntary respiration Two

- Voluntary hypervent. : Stops due to -- arterial PCO_2 .
- Voluntary apnea (breath holding) For 45-60 second. Ends at break point due to -- arterial PO_2 & ++ arterial PCO_2

Duration of voluntary breath holding can be prolonged by:

- Initial hypervent : prolonged apnea for 15-20 sec due to -- PCO_2
- Prior inhalation of pure O_2 for 1 min : prolongs apnea 5 min
- Holding breath in full inspiratory position : inhibits respiratory centre by impulses from pulm. stretch receptors.
- Some visceral reflexes e.g. swallowing

Hypothalamus integrate visceral and somatic functions

- Parasymp. centres e.g. in severe pain inhibit respiration
- Sympath. centres e.g. in emotions stimulate respiration
- Temp. regulating centres e.g. in fever stimulate respiration

2 Afferents from respiratory mechanoreceptors

- Upper respiratory passages Irritant receptors

	<u>Coughing</u>	<u>Sneezing</u>
<u>Site</u>	irritation of mucosa of trachea, larynx & bronchi	irritation of mucosa of nose
<u>Afferents</u>	<u>Vagus</u> nerve	<u>Trigeminal</u> nerve
<u>Stimuli</u>	<u>Mechanical</u> : dust particles, mucus or food <u>Chemical</u> : cigarette smoke or irritant gases	
<u>Response</u>	<u>Deep inspiration</u> followed by forced expiration against closed glottis (abdom p 100 mmHg)	
	<u>suddenly opened</u> → air velocity several hundred Km/hour	<u>Opened</u> glottis Post. nasal opening is closed by elevated soft palate. (7)

2 Lungs 2 types slowly & rapidly adapting recept. SAR₃ Afferent SL

A Lung stretch receptors Slowly adapting receptors

Site Airway smooth muscle.

Afferent Vagus nerve (Hering Breuer reflex)

Stimulus lung inflation & airway distension.

Response Inhibitory impulses to APC & DRG

Aim Protective mechanism which prevents overventilation rather than controlling normal rate and depth of breathing

B Lung irritant receptors Rapidly adapting receptors

Site mucosa of bronchi & bronchioles (extension of those of upper air)

Afferents Vagus nerve.

Stimuli Mechanical : dust & particles

Chemical : exogenous e.g. smoke or endoge. ... e.g. histamine

Response Coughing, bronchoconstriction and apnea.

C Juxta pulm. capillary receptors (J receptors) RAR

Site Alveolar wall close to pulmonary capillary

Afferents Vagus nerve

Stimuli ++ pulm. interstitial fluid p or capillary pressure
e.g. pulm. congestion in L-sided HF failure & pulm. embolism

Response Tachypnea (rapid shallow breathing) & dyspnea.

3 Afferent from chest wall receptors

Site located in chest wall muscles and their tendons

Afferent Vagus nerve

Stimulus Chest wall expansion (force generated by resp. muscles)

Response Send inhibitory impulses which determine tidal volume.

Increased respiratory effort to distend the lung (due to ++ air way resistance or -- compliance), the information from these receptors give rise to dyspnea.

Afferent from proprioceptors in sk ms, tendons, joints & ligaments
Stim. ventilation during muscular exercise

Afferents from CVS

Respiratory & circulatory systems are integrated; because O_2 supply & CO_2 removal require adequate ventilation and perfusion.

Arterial baroreceptors

High pressure receptors

Site Aortic arch & carotid sinus

Afferent Bulbar nerves (IX & X)

Stimulus ABP & PP

Response ++ ABP $\rightarrow$ -- respiration
i.e. inhibitory impulses

e.g. adrenaline apnea

Ageing, -- ABP $\rightarrow$ ++ respiration

Atrial receptors

Low pressure receptors

Rt atrium & big veins

Vagus nerve

Central venous pressure e.g. VR

++ VR $\rightarrow$ ++ CVP $\rightarrow$ ++ respiration

i.e. excitatory impulses to RC

called Harrison's reflex.

Bainbridge reflex

6 Visceral reflex

a Swallowing

Site & stimulus Food stimulates receptors in mucosa of pharynx

Afferents Glossopharyngeal nerve.

Response Glottis is closed + temporary swallowing apnea

Similar apnea occurs during vomiting & straining.

b Hiccup

Cause Irritation of phrenic nerve.

Response Spasmodic cont. of diaphragm $\rightarrow$ inspiration during which glottis suddenly closes $\rightarrow$ characteristic sound & sensation

Treatment often respond to breath holding $\rightarrow$ ++ arterial PCO_2

c Yawning Physiological basis are uncertain, it tends to open collapsed undervent. alveoli & also ++ venous return

Hypoxia

Definition O₂ deficiency at tissue level.

Types of hypoxia

Types Items	Most common <u>Hypoxic H.</u>	<u>Anemic H.</u>	<u>Stagnant H.</u>	<u>Histotoxic H.</u>
<u>Arterial PO₂</u>	--	normal	normal	normal
<u>Functional Hb</u>		--	normal	normal
<u>Bl. Flow to tissues</u>			--	normal
<u>Oxidative Enzyme</u>				(poisoning)
<u>Causes</u>	1 -- PO₂ in insp air e.g. High altitude 2 Pulm. disorders - a impaired ventilat. 1 -- of resp. centre 2 Obstructive disease e.g. br. asthma 3 Restrictive diseases e.g. fibrosis or collapse - b impaired diffusion thick pulm. mem. - c impaired ventil. perfusion ratio 3 Shunt of venous to arterial blood	1 Quantitative ↓ e.g. anemia 2 Qualitative ↓ e.g. CO poisoning refer to page 11	1 Generalised e.g. H. failure circ. shock 2 Localised e.g. thrombosis embolism	1 <u>Cyanide poison</u> ↓ cytochrome oxidase remained reduced 2 <u>Alcohol and narcotic poison</u> block dehydroge- nase enzyme Cytochrome remains oxidized.
<u>Characters:</u>				
<u>Arterial PO₂</u>	--	normal	normal	normal
<u>,, O₂ content</u>	--	--	normal	normal
<u>,, % sat of Hb</u>	--	normal	normal	normal
<u>Venous PO₂</u>	--	--	--	++
<u>,, O₂ content</u>	--	--	--	++
<u>,, % sat. of Hb</u>	--	--	--	++
<u>Cyanosis</u>	Present	Absent	Present	Absent
<u>2 therapy</u>				(10)
<u>Chemical O₂</u>	Increased		No ++	No ++
<u>Physical O₂</u>	++	++	++	++ no benefit

CO₂ poisoning (carboxy Hb)

Sources: incomplete combustion of carbon or gasoline

CO is toxic because: 1. carboxy Hb. can't carry O₂.

2. affinity of Hb to CO is 210 times that for O₂.

3. Carboxy Hb shifts O₂ diss. curve to Lt i.e. ++ affinity of Hb to O₂.

4. " Hb breaks down slowly.

Sign Carboxy Hb is cherry red colour. (skin & mucous mem.)

tlc 1. Termination of exposure 2. Artificial respiration.

3. O₂ therapy [a] A pure O₂ → ++ physical O₂ → ++ P_{O₂}

[b] Hyperbaric O₂ 1-3 atmospheric pressure

[c] 95% O₂ + 5% CO₂ is better because:

- CO₂ stimulates resp. - CO₂ -- affinity of Hb to CO.

4. Blood transfusion.

• Met Hb Hb (ferrous) oxidizing agent → Met Hb (ferric)

Signs Met Hb dull grayish colour appears in skin & mucous mem.

• Sulf Hb rare caused by reducing agent

Signs bluish leaden colour

Note Rate of O₂ diff. depends on P_{O₂} in capill. bl. (which is the average of P_{O₂} in arterial and venous bl.).

Oxygen therapy

Highly beneficial in

Less beneficial in

Not beneficial in

1. Hypoxic H due to

1. Hypoxic H due to

Histotoxic H.

-- atmosph. P_{O₂}

A-V shunt

Hypoventilation

Impaired diffusion

2. Anemic H

2. CO poisoning

3. Stagnant H

Oxygen toxicity

Cause O₂ free radicals oxidizing cell mem & enzymes leading to:

1. Oxidative destruction of enzymes 2. Damage of nervous tissue

A) Pure O₂ - 8 H or more causes irritation of upper air ways